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Murine typhus in children: clinical and laboratory features from 41 cases in Crete, Greece

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Murine typhus, also known as endemic typhus, is a flea-borne infectious disease with a worldwide distribution, caused by an obligate intracellular, gram-negative microorganism, *Rickettsia typhi* [1]. The transmitting agent of *R. typhi* is the rat flea, *Xenopsylla cheopis*, although the cat flea, *Ctenocephalides felis*, has also been implicated [1–4]. Main reservoirs are rats, house mice, opossums, skunks and cats [1–3]. The actual incidence of murine typhus is unclear, as the common clinical manifestations of the disease are non-specific [1,2]. In children, only a small number of studies have focused on the occurrence and on clinical profiles of the disease [3–5]. The aim of this study was to confirm the presence and to assess the clinical and laboratory characteristics of *R. typhi* infection among children in the area of Chania, Crete, Greece.

Forty-one children were hospitalised with acute *R. typhi* infection in the Pediatric Department of the General Hospital of Chania, from 2001 through to 2006. All other causes included in the differential diagnosis were ruled out. Diagnosis of acute *R. typhi* infection was considered positive by the combination of compatible clinical features and an indirect immunofluorescence test (Biomerieux, Lyon, France), when specific IgM and/or IgG titres on admission were >1/400 and >1/960, respectively. All cases were reviewed retrospectively for demographic, clinical and laboratory findings, treatment and outcome.

Most admissions (87.8%) occurred between May and October. The mean age was 9.8 years old (range, 1–15 years old). Twenty children (48.8%) were males. History of recent contact with animals was positive in 13 children (31.7%); all 13 children reported contact with cats and 10/13 reported contact with dogs. On admission all patients had fever. Common clinical characteristics were fever, rash, hepatomegaly, splenomegaly and anorexia. Main laboratory features included elevated aspartate aminotransferase and alanine aminotransferase, abnormal chest radiography, thrombocytopenia and leucopenia. CSF analysis in one patient with confusion did not reveal any abnormalities. Clinical and laboratory manifestations found on admission are presented in Table 1.

Serologic testing through IFA performed on admission was diagnosed for all 41 children, with a median IgM titre of 1/3200 (range, 1/400 to 1/31200) and a median IgG titre of 1/2880 (range, 1/480 to 1/30720).

All children were treated upon admission. Combination therapy was administered to two of them. Antibiotics administered were doxycycline in 19 children (46.3%), chloramphenicol in 12 (29.3%), quinolones in five (12.2%), cephalosporins in three children (7.3%), and a combination of trimethoprim/sulfamethoxazole and b-lactams in two children (4.9%).

The outcome was favourable for all 41 patients; apyrexia was recorded on a mean of 4.9 days after admission (range, 2–12 days). The mean total duration of fever was 9.1 days (range, 3–17 days). No complication or relapse was observed within 1 month of follow-up.

DISCUSSION

The temperate climate of the Mediterranean basin is a major contributing factor to the endemicity of murine typhus in the area [1–4]. Only a few studies have described flea-borne typhus in chil-

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Table 1. Clinical, epidemiological and laboratory characteristics of murine typhus in 41 children in Chania, Crete

Clinical characteristic	
Fever	**41 (100.0)**
Rash	26 (63.4)
Macular	14 (34.9)
Maculopapular	12 (27.9)
Hepatomegaly	25 (61.0)
Chills	25 (60.0)
Perspiration	20 (48.8)
Splenomegaly	19 (46.3)
Anorexia	17 (41.5)
Malaise	15 (36.6)
Myalgia	13 (31.7)
Joint pain	11 (26.8)
Abdominal pain	6 (14.6)
Headache	6 (14.6)
Lymphadenopathy	5 (12.2)
Cervical	4 (9.8)
Submandibular	1 (2.4)
Diarrhoea	4 (9.8)
Cough	4 (9.8)
Vomiting	4 (9.8)
Confusion	1 (2.3)

Laboratory findings	
AST > one-fold[a]	**30 (73.0)**
ALT > one-fold[a]	27 (65.6)
Abnormal chest radiography	22 (53.7)
Thrombocytopenia[b]	16 (39.0)
Leucopenia[c]	10 (24.4)
Proteinuria	7 (17.0)
Haematuria	6 (14.6)
Hyponatraemia[d]	4 (9.8)
Other characteristics	
Male sex	20 (48.8)
Recent contact with animals	13 (31.7)
Mean duration of fever before admission (range)	5.7 days (1–15 days)
Mean duration of fever (range) after admission	9.1 days (3–17 days)
Rash onset after fever (mean, range)	3.6 days (1–8 days)
Total rash duration (mean, range)	4.7 days (2–9 days)

AST, aspartate aminotransferase; ALT, alanine aminotransferase; [a]normal value, 0–40 U/L; [b]normal value, 150–450 × 10^9/L; [c]normal value, 5–10 × 10^9/L; [d]normal value, 135–145 mEq/L.
Values given are *n* (%).

dren, and differences in the clinical presentation of the disease among children and adults need further investigation [2–5].

In our study, the main clinical manifestations were fever, rash, chills, perspiration, anorexia and hepatosplenomegaly, which is in agreement with other studies involving children [3–5]. In contrast to adults, headache (14.6%), the classic triad of fever, headache and rash (12.2%), and conjunctivitis (none), were uncommon in our study [2]. Pulmonary involvement was much more common in children (53.7%), while hyponatraemia was observed only in a small number of children (9.8%), compared with adults [2].

The clinical course of the disease in our cases was mild and without complications. A possible explanation is the early administration of the appropriate therapy, due to increased medical awareness in Crete, where murine typhus is endemic [2,3].

In conclusion, murine typhus in children causes a mild disease, presenting with non-specific clinical features. Clinical and laboratory characteristics of the disease present certain diversities when compared with murine typhus in adults. Therefore, when related epidemiological information is available, fever, rash, anorexia and hepatosplenomegaly in children should raise suspicion for *R. typhi* infection.

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